UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,946	08/08/2001	Mark J. Evans	0630/1G703US2	3104

7278 7590 06/07/2005

DARBY & DARBY P.C.
P. O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,946	EVANS ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15,17-29,37-41 and 45-68* is/are pending in the application.

4a) Of the above claim(s) *21-29,37-41,45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10,13-15,17-20,47-57 and 62-68* is/are rejected.

7)☒ Claim(s) *11,12 and 58-61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on February 23, 2005, amending claims 8, 13, 18, 47, 48 and 49, canceling claims 1-7, 16 and 30-36 and adding claims 56-68, has been entered.

Claims 8-15, 17-29, 37-41 and 45-68 are pending. Claims 21-29, 37-41 and 45-46 are withdrawn. Claims 8-15, 17-20 and 47-68 are under consideration.

Claim Objections

Applicant is advised that should claims 47-50 be found allowable, claims 48-50 will be objected to under 37 CFR 1.75 as being a substantial duplicate of claim 47. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Response to Arguments

Applicant's amendment and arguments filed on February 23, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Examiner acknowledges applicants arguments regarding the rejection of claims 8-10, 13-15, 17-20 and 47-55 under 35 U.S. C. 102(g).

Claim Rejections - 35 USC § 112

Claim 13 and claims 14-15 and 17 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 13, the phrase "any combination thereof" is not clear. The metes and bounds are not clear in the context of the claims. It is not clear to the Examiner what combinations applicants are referring to.

Claim 18 and claims 19-20 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 18, the phrase "corresponding to " is not clear. The metes and bounds are not clear in the context of the claims. The specification does not describe as to how one skilled in the art can determine as to which specific hybridization condition "corresponds to" the condition recited in the claim. Therefore, it is unclear from the specification or from the claims as to what applicants mean by the above phrase. Examiner suggests direct reference to the hybridization condition.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10, 13-15, 17-20, 47-57 and 62-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding the EER-7 of SEQ ID NO:2, vectors and host cells comprising said polynucleotide and a method of producing said EER-7 protein, does not reasonably provide enablement for (A) polynucleotides encoding EER-7 or a fragment of EER-7 having 75-95% sequence identity to SEQ ID NO:2, having four copies of a scavenger receptor cysteine rich domain (SRCR) having at least 80% sequence identity to any one of SEQ ID NOs: 3-6 or (B) oligonucleotides comprising 1-100 nucleotides, wherein the oligonucleotides comprises of at least 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizes under the conditions recited in claim 18 . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 8-10, 13-17, 47-55, 62-64 and 66-68 are drawn to polynucleotides encoding EER-7 or a fragment of EER-7 having 75-95% sequence identity to SEQ ID

NO:2, having four copies of a scavenger receptor cysteine rich domain (SRCR) having at least 80% sequence identity to any one of SEQ ID NOs: 3-6. Claims 18-20, 56-57 and 65 are drawn to oligonucleotides comprising 1-100 nucleotides, wherein the oligonucleotides comprises of at least 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizes under the conditions recited in claim 18. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding EER-7 polypeptides and oligonucleotides, hybridizing to SEQ ID NO:1 under conditions recited in claim 18, broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide encoding the EER-7 protein of SEQ ID NO:2 having lysyl oxidase activity and the oligonucleotides consisting of SEQ ID NOs: 8-10 or 11. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and oligonucleotides. In view of the great breadth of the claim, amount of experimentation required to make and used the claimed polynucleotides and oligonucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and

Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495 - Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any EER-7 protein with 75-95% identity to SEQ ID NO:2 and comprising of four SRCR domains having any one of SEQ ID NOs: 3-6 and oligonucleotides comprising of 1-100 nucleotides comprising of any 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizing to SEQ ID NO:1 because the specification does not establish: (A) regions of the encoded EER-7 protein structure which may be modified without affecting lysyl activity; (B) the general tolerance of EER-7 proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the

desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides encoding EER-7 proteins with an enormous number of amino acid modifications of the EER-7 protein of SEQ ID NO:2 and oligonucleotides comprising of 1-100 nucleotides comprising any 20-30 nucleotides of SEQ ID NO:1 . The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides encoding EER-7 having the desired biological characteristics and determination of oligonucleotides comprising any 20-30 consecutive nucleotides of SEQ ID NO:1 are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that the claims are drawn to polynucleotides encoding EER-7 proteins having related structure since the claims recite the limitation that the encoded polypeptide comprise the catalytic domain of SEQ ID NO:1. While that may be so, Examiner respectfully disagrees that such arguments are persuasive to overcome the rejection. The catalytic domain of the encoded EER-7 protein only amounts to 30% of the whole structure EER-7 and 80% of any four copies of SEQ ID NOs:3-6 amounts to

only 42-50% of the whole structure of EER-7. Therefore, the claims are drawn to polynucleotides encoding 75%-95% of the entire structure of EER-7 and the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding EER-7 polypeptides broadly encompassed by the claims. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides.

Applicants also argue that since the claims are drawn to polynucleotides encoding EER-7 proteins having 100% sequence identity to the catalytic domain of EER-7, it is routine experimentation alter the amino acid sequence of a protein and still obtain a protein with similar protein activity. Examiner respectfully disagrees. The specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in retaining its activity are limited in any protein and the result of such modifications is unpredictable. Even a single mutation in a protein is known to affect correct folding of the mutant protein and affect its catalytic activity (Lascu et al. – form PTO-892). Therefore, without specific guidance as to which amino acids can be modified, it is unpredictable if a mutant protein having modifications of 5-25% of the structure of SEQ ID NO:2 will retain its activity. While the art may teach in general the structure of EER-7 and its catalytic domain, conserved amino acid sequences, and etc, such teachings will not reduce the burden of undue experimentation on those of ordinary skill in the art.

Applicants also argue that one skilled in the art would appreciate the amount of diversity that would establish general tolerance to modification based on highly

developed state of the art in making recombinant DNA and mutagenesis techniques. While that may be so, that knowledge by itself is not sufficient to make modifications as claimed in the instant claims. The claims encompass polynucleotides encoding any mutant, variant or recombinant of SEQ ID NO:2, having 5-25% amino acid modifications.

Applicants also argue that there is ample guidance in making and using oligonucleotides since the claims limit the oligonucleotides to 100 nucleotides that hybridize to SEQ ID NO:1 under stringent conditions and making such oligonucleotides is routine. While making oligonucleotides from a given polynucleotide may be routine in the art, the claims encompass an extremely large number of oligonucleotides. It would require undue experimentation of the skilled artisan to use oligonucleotides that consists of 1-100 nucleotides comprising any 20-30 nucleotides of a polynucleotide sequence having 2600 nucleotides that also hybridizes to SEQ ID NO:1 under stringent conditions. Hence the rejection is maintained.

Claims 13, 18-20, 56-57 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are direct to a genus of oligonucleotides that consists of 1-100 nucleotides comprising 20-30 nucleotides of SEQ ID NO:1. The specification does not

contain any disclosure of the function of all the oligonucleotides that consists of any 20-30 nucleotides of SEQ ID NO:1. The genus of these polynucleotides that comprise these above oligonucleotide molecules is a large variable genus with the potentiality of having any function or no function. Therefore, many functionally unrelated oligonucleotide are encompassed within the scope of these clams, including partial DNA sequences. The specification discloses only a few species of the claimed genus (i.e. primers consisting of the oligonucleotide of SEQ ID NOs: 8-10 or 11) which is insufficient to put one o sill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter

Claims 11-12 and 58-61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Examiner 1652